REMARKS

Applicants thank the Examiner for the detailed analysis of the pending claims and application. With respect to the objections to the drawings, attached are drawings with proposed corrections. Attention is respectfully directed to Figure 16 in which anchoring sutures for the refill port are added; this is supported by paragraph 0119 of the published version of the present application. Referring to Figure 18, part number 49 is replaced by 44. The specification is amended to delete part number 49. With respect to Figure 19, the second cavity and corresponding refill port and tube were added; these features are also supported by numerous references in the specification as filed. If there are any further changes desired or concerns with the proposed changes, it is respectfully requested that the Examiner telephone the undersigned to expedite submission of drawings acceptable to the Examiner. To the extent the Examiner believes any amendments to the specification are needed as a result of this amendment, the undersigned is authorized to agree to Examiner's amendments via telephone conference consistent herewith.

With respect to the terminal disclaimer requirement, the undersigned has been authorized to prepare and submit same as soon as all other substantive issues are resolved; compliance with this requirement is deferred in order to focus on reaching agreement on claims that are patentable over the prior art.

The amendment to Claim 4 is supported by paragraph [0084] of the published version of the present specification (page 12, line 3 of the original specification). The term valve is used in the specification to describe a fitting (an example of which is shown in Figure 17) that is fixed in the wall of the device housing and used to connect the reservoir in the housing to a refill tube that is connected to a refill drum. Claims 14, 46, 47 and 50 are canceled hereby without waiver in order to expedite prosecution. The term crossing band is in original claim 39 and is supported by paragraph [0159] *inter alia*.

With respect to the rejections based on 35 USC 102 and 103, it is respectfully submitted that the amendment to claim 1 recites an important sealing features that solve a problem not recognized or solved by the prior art. The remaining claims recite additional distinctions. Attention is respectfully directed to the prosecution history of the parent application from which priority is claimed. In particular, applicants discovered

that in order to minimize undesired side effects of highly toxic therapeutic materials, it is necessary to carefully control their delivery to a target. This requires that the release port be the only substantial release point for therapeutic materials. By use of adhesives in a well defined structure that blocks undesired spreading thereof and/or sutures, important improvements in drug delivery are achieved.

With reference to the cited Urquhart patent, there is no recognition of the importance of holding an adhesive in place to seal a device perimeter to a target tissue, such as the eye, in order to avoid leakage of the adhesive across the drug-tissue interface [column 9, paragraph 2 of Urquhart]. If Urquhart's device were implanted to the ocular sclera, for example, properties of the sclera as a permeable membrane would have been diminished or lost and reproducibility of drug distribution in targeted tissue would vary widely according to the ability of the surgeon to implant the device with minimal adhesive spread into the drug-tissue interface. Most adhesives used as tissue glue (e.g. butyl-acrylate and cyanoacrylate) could not be used as they polymerize and form a very impermeable layer of acrylic on the moist surface of the targeted organ/tissue. Urquhart does not recognize the need to use a buckle or a suture holding mechanism on his device that facilitates a hermetical seal to a targeted tissue. In contract, the present inventors have conducted and published studies demonstrating the superior delivery of drugs using the presently claimed inventions (e.g., Published manuscript, IOVS 2006).

With respect to the Theeuwes patent, an implantable patch is disclosed. Theeuwes does not recognize the need for attachment mechanisms that create a firm, substantially leak-free seal with a target tissue. In contrast, the presently claimed device can be used to apply commercially available liquid tissue adhesives, such as INDERMIL (Covidien Corp., Mansfield, MA, U.S.A.) and DERMABOND (Ethicon Corp., New Jersey, U.S.A.). Use of such adhesives with the prior art devices would result in an undesirable risk of leakage into the drug-tissue interface that would impair the ability of the drug to diffuse across the tissue.

Turning to the Avery patent, an intravitreal device is disclosed for implantation outside of the eye; it is secured to the eye by suture tabs by standard anchoring sutures (columns 9 and 10). Some parts of the device can be rigid to avoid compression by the movement of the eyelids. Avery's device can be placed outside the eye but delivers the

drug through a direct communication through the inside of the eye (vitreous cavity), therefore the diffusion is controlled by the factors determined by the open end of the intravitreal portion of the system. Avery does not recognize the permeability properties of the sclera nor the need for attachment mechanisms to hermetically seal a device to a tissue surface. Avery does not recognize the need to seal the perimeter of the drug diffusion window to tissue and instead allows drug to be freely released into the vitreous cavity; the vitreous is a gel barring the controlled diffusion that the present invention can accomplish.

With respect to Yamamoto, Jones and Finch, none teach how to make a drug delivery device that can be hermetically sealed to a target tissue, such as the eye. Should the Examiner believe there are further issues that need to be resolved prior to allowance, one or more of the Applicants would be pleased to meet with the Examiner to expedite prosecution.

Respectfully submitted,

2008 November 21
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